years ago, first clinical trials on safety and immunogenicity. In the meantime more than 25,000 women have been included into several efficacy trials which demonstrated protection against persistent infection with HPV 16 and 18 and against the development of precursor lesions to cervical cancer. Although the ultimate proof of success, i.e. reduction of cancer incidence still requires the immunization of large populations and many years of follow-up, the existing data are so persuasive that the first marketing of the vaccine is expected to be announced in mid 2006. Yet several questions such as the duration of protection, the need development of for post-exposure vaccination strategies and availability of such vaccine in low-budget countries are open and will be discussed.

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## S39. IDENTIFICATION OF POTENTIAL TARGET ANTIGENS FOR IMMUNOTHERAPY APPROACHES

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Immunotherapy approaches in cancer rely on the identification of suitable antigens that can be used as targets for therapeutic approaches. The ideal target antigen is highly and homogenously expressed in cancer, but not or low level expressed in normal tissues. Using different cloning techniques, several potential target antigens have been identified, some of these antigens are already being evaluated in clinical trials. We followed a cloning strategy called SEREX that identifies tumor antigens based on a spontaneous humoral immune response in patients. Using this technique we identified 2 new tumor associated antigens that belong to the group of differentiation antigens: NY-BR-1 as a new breast differentiation antigen and RAB38/NY-MEL-1 as a new melanocyte differentiation antigen.

NY-BR-1 is not expressed in normal tissues except in normal mammary gland and testis, but it is highly expressed in 70% of breast cancers. Antigen positive cancers maintain the expression in metastatic lesions. Spontaneous antibody responses occur in about 10% of breast cancer patients. We identified 2 HLA-A2 restricted NY-BR-1 derived epitopes that were recognized by CD8+ T cells from patients with NY-BR-1 expressing cancers. Both epitopes are naturally processed and presented.

RAB38/NY-MEL-1 is expressed in melanocytes and at low level in adrenal gland, all other normal tissues are RAB38/NY-MEL-1 mRNA negative. Spontaneous humoral immune responses are frequent in melanoma patients but not in normal individuals, in patients with vitiligo or with cancers other than melanoma. We recently identified a HLA-A2 restricted RAB38/NY-MEL-1 derived epitope that is naturally processed and presented and recognized by CD8 T cells.

Both new antigens, NY-BR-1 and RAB38/NY-MEL-1 are being evaluated as targets for T cell based immunotherapy strategies in Phase-I trials.

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## S40. T CELL BASED IMMUNOTHERAPY – CHANGES AND CHALLENGES

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Advances in cellular and molecular immunology have led to the development of strategies for effective augmentation of anti-tumor immune-responses in cancer patients. This presentation focuses on the manipulation of T cell immunity either by active-specific immunization with tumor vaccines[1–4] or by adoptive immunotherapy with immune T cells.[5,6] Such therapies offer exquisite specificity of tumor recognition based on the ability of the T cell to distinguish single amino acid differences in any protein from any compartment of the tumor cell.

Recent analyses of bone marrow samples from patients with a variety of different cancers revealed the existence of cancer reactive memory T cells in a high proportion and at high frequencies.[5–9] A fine specificity analysis revealed *individuality* (i) of response patterns to multiple tumor associated antigens (TAAs), (ii) of the size and (iii) of the specificity of the memory repertoire in the bone marrow of cancer patients. These findings challenge immunotherapy approaches targeting single TAAs. Future strategies will be discussed for the exploitation of the TAA memory repertoire of cancer patients. In "proof of principle" studies it was demonstrated to have great therapeutic potential.[5,6]

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## S41. TARGETING THE APOPTOTIC PATHWAY TO INDUCE RADIORESISTANCE IN NORMAL TISSUE AND STEM CELLS

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Novel strategies in clinical radiotherapy have the goal to increase the therapeutic index i.e. effective tumor cell kill while sparing the normal tissue. This can be achieved by either physical selectivity when the tumor is well circumscribed or by biological selectivity when normal tissue is present in the treatment volume. Biological selectivity can be achieved by targeting tissue properties which are only present either in tumor or normal tissue cells.

Radiation induced apoptosis is a rare event as compared to mitogenic death in epithelial tumor cells. In contrast, radiation